REMARKS

Claims 1-28 are pending in the application, and the Examiner has rejected claims 1-28. Claims 1 and 14 have been amended. Claims 6, 8, and 17 have been canceled. Claims 1-5, 7, 9-16, and 12-28 remain herein for consideration.

Claim Rejections

The Examiner rejects claims 1-2 and 8-12 as anticipated by, or in the alternative, as obvious over Johnson, et al., U.S. Patent No. 5,947,921, either alone or in view of Alvarez and Doan, et al.

The Examiner states that Johnson, et al. teaches simultaneous application of ultrasound in the range of less than 2.5 MHZ and in the 0-1 W/cm^2 and up to 1 mA/cm^2. The Examiner states that Applicants have not set forth any particular parameter ranges in their specification in which dermal matrix protein generation is limited but merely describe preferred ranges. The Examiner further states:

> Notwithstanding, from the scope of claims 1 and 14, it would appear that any combination of ultrasound and electrical energy produce collagen generation. Johnson meets this criteria. Moreover, Johnson applies combinations of ultrasound and electrical energy in applicant's preferred ranges and thus the examiner concludes the Johnson drug delivery method would also inherently result in collagen production. It is noted that a discovery of a result that is not explicitly stated in a known method is not considered patentable over the known method.

The Examiner further states:

> Alternatively, to have realized that the combination of the Johnson application would have inherently result in collagen synthesis would have been obvious in view of the teachings of Doan

et al and Alvarez that teach the synthesis of collagen within the Johnson et al parameter ranges.

Claim 1 has been amended to add range limitations directed towards the electrical current and ultrasound frequency:

> wherein a current of said electrical energy is about 100 microamps; and wherein said ultrasound is provided at a frequency in a range of about 1 to about 4 megahertz.

Johnson et al. is not directed towards the stimulation of production of extracellular dermal matrix proteins in human tissue as is Applicants' process claim 1. Instead, Johnson et al is specifically directed to enhancing the penetration of superficial skin layers by such medicines as Corticosterone, Dexamethasone, and Testosterone. Further, as amended, claim 1 claims a process of simultaneously delivering ultrasound and electrical energy in ranges not specified by Johnson et al. Johnson et al. teaches the application of an electrical current . . . at a current density of greater than zero up to about 1 mA/cm2. In contrast, Applicants' amended claim 1 calls for an electrical current of about 100 microamps, which, although not a current density, is an order of magnitude less than the current referenced in Johnson et al. Finally, with regard to ultrasound frequency, Johnson et al. teaches that "'low frequency' sonophoresis is ultrasound at a frequency that is less than 1 MHZ, more typically in the range of 20 to 40 kHz." In contrast, Applicants' amended claim 1 requires that, "said ultrasound is provided at a frequency in the range of about 1 to about 4 megahertz." Since Applicants' amended claim 1 calls out parameters not taught by Johnson et al. for a purpose not contemplated by Johnson et al., Applicants submit that amended claim 1 is not obvious over Johnson et al. alone.

Further, amended claim 1 is not obvious over Johnson et al. in view of Alvarez and Doan.

As explained above, Johnson et al. teaches application of electrical current and ultrasound for a different purpose and in different ranges than does applicant. Alvarez teaches the healing of superficial skin wounds by external electrical current. Doan teaches the application of ultrasound to human gingival fibroblasts, mandibular osteoblasts , and monocytes in vitro at frequency ranges of 1 MHZ and 45 kHz. The Applicants' invention does not use direct current on superficial wounds. In contrast, Applicants' invention uses high frequency electrical pulses in combination with ultrasound acoustic energy to penetrate dead outer layers of skin to directly stimulate growth and regeneration of collagen located below the surface of the skin. The detailed description of the mechanism by which this occurs, as well as specific application parameters are taught in the specification.

Applicants' claim 1, unlike Alvarez, claims the stimulation of production of extracellular dermal matrix proteins in human tissue. Unlike Doan, Applicants claim the application of ultrasound energy at a frequency in the range of about 1 to about 4 megahertz, which is outside the range of frequencies considered by Doan.

Applicants' claim 1 is not obvious over Johnson et al. in view of Alavarez and Doan because neither Johnson et al., Doan nor Alvarez teach or suggest, alone or in combination, the application of electrical energy and ultrasound in the specified ranges to achieve a process for the stimulation of production of extracellular dermal matrix proteins in human tissue. Further, none of the references teach the unexpected results achieved by Applicants' combination of the application of

electrical and ultrasound energies as set forth by Applicants on page 11, lines 12 and 13 as follows: "When these energy sources are used simultaneously to stimulate, the resultant tissue matrix formation will be improved as compared to using either modality independently."

Dependent claims 2 and 8 - 12 all depend, at least indirectly, from amended independent claim 1, which is submitted to be patentable. The dependent claims are therefore also submitted to be patentable.

Claim Rejections - 35 U.S.C. § 103(a)

The Examiner rejects claims 1-2 and 7-13 over Johnson, et al., U.S. Patent No. 5,947,921, either alone or in view of Alvarez and Doan, et al., and are rejected as being unpatentable over Henley, U.S. Patent No. 5,538,503, in view of Johnson, et al., U.S. Patent No. 5,947,921.

The Examiner states that Henley teaches the application of electrical energy in the form of pulsed waves of 10-300 Hz, 10-40 volts in combination with ultrasound but does not teach Applicants' preferred power or ultrasonic frequency range. The Examiner further states that Johnson teaches standard frequency rages and power levels for drug delivery that correspond to the preferred ranges taught by Applicants. The Examiner concludes, "To have used these ranges would have been obvious since they are standard in the art for delivering drugs and would inherently generate collagen in accordance with applicant's disclosures."

Henley is specifically directed to improving the penetration of a drug by application of electrical energy at different parameters than that of Applicant . For this reason and the reasons set forth above with respect to Johnson et al., Alvarez and Doan, Applicant asserts that claims 1-2 and 7-13 are patentable over Johnson, et al., either alone or in view of Alvarez and Doan, et al., and over Henley, in view of Johnson, et al., U.S. Patent No. 5,947,921.

Claim Rejections - 103(a)

The Examiner has rejected claims 1-28 as being unpatentable over Zhang, et al. in view of Johnson and further in view of Alvarez and Doan. The Examiner states:

> While Zhang et al teaches the application of ascorbic acid to wounds in the background of the invention, and teaches that ultrasound may be administered simultaneously along with iontophoresis and electroporation (column 9 lines 45-50) with electrical pulsing with in applicant's disclosed frequencies and field strength he does not teach the application of his electroporation/ultrasound in applicant's preferred ultrasound range or a method of treating a preexisting wound. However, as noted above, to have used the ultrasonic frequencies and power settings of Johnson would have been conventional to achieve better drug delivery. In addition the examiner considers it obvious to have applied the method to a wound that was created by injury since his method deals with healing the skin via collagen formation. Alternatively to have produced a wound in the skin to test the healing capabilities of the Zhang et al method would have been obvious in view of the teachings of Alvarez who induces keratome wounds in test animals for purposes of testing the collagen synthesis capabilities of his method. To have realized the further benefits of ultrasound of wound healing as taught by Doan et al would have been obvious.

Neither Zhang, Johnson, Alvarez nor Doan teach or suggest, either alone or in combination Applicants' claimed process as set forth in Applicants' amended claims 1 and 14, which set forth specific parameters for the application of electrical and ultrasound stimulation. The Applicants' combination of stimulation and ultrasound results in the surprising result of a greater stimulatory effect achieved by the combination of electrical and ultrasound stimulation than may be achieved through either the application of electrical current or ultrasound, as noted above. Further, Applicants' device stimulates fibroblasts of soft tissue to become collagen 1, 3 elastin and reticulin. All of the Examiner's cited references point to a potential to stimulate collagen. However, collagen has numerous forms such as large bundle and smaller more resilient fibers, as well as elastin and reticulin. Applicants' invention effects all of the above types of collagen to form a tissue matrix that resembles normal healthy tissue. In contrast, the stimulation of just collagen 1 will result in scar tissue formation. Applicants' invention is superior to prior art teaching in that Applicants' invention results in formation of a collagen matrix that more closely resembles normal healthy tissue.

A further distinction of the Applicants' invention is that the Applicants combine a specific electrical waveform and a specific consistent and accurate ultrasound to stimulate collagen, elastin, and reticulin. While Doan teaches that ultrasound may have a positive effect on the stimulation of collagen, the Applicants' invention is directed toward the idea that electrical stimulation stimulates collagen 1 and the application of ultrasound stimulates collagen 3 and elastin and reticulin. The Applicants' invention involves the combination of specific parameters of electrical stimulation and ultrasound to stimulate all the elements of the tissue matrix.

* * * * *

This paper is intended to constitute a complete response to the outstanding Office Action. Please contact the undersigned if it appears that a portion of this response is missing or if there remain any additional matters to resolve. If the Examiner feels that processing of the application can be expedited in any respect by a personal conference, please consider this an invitation to contact the undersigned by phone.

Respectfully submitted,

6/1/04
DATE

SIGNATURE OF PRACTITIONER

Reg. No.: 36,050

R. Alan Weeks
(type or print name of practitioner)

Tel. No.: (918) 599-0621

321 S. Boston Ave., Suite 800
P.O. Address

Customer No.: 22206

Tulsa, OK 74103-3318